

Received: 2021.02.21

Accepted: 2021.04.27

Available online: 2021.05.11

Published: 2021.06.12

# Aortic Angiosarcoma in Association with Endovascular Aneurysm Repair: Case Report and Review of the Literature

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Statistical Analysis C  
Data Interpretation D  
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**Conflict of interest:** None declared

**Patient:** Female, 82-year-old  
**Final Diagnosis:** Angiosarcoma of the aorta  
**Symptoms:** Fever  
**Medication:** —  
**Clinical Procedure:** —  
**Specialty:** Pathology

**Objective:** Rare disease


**Background:** Primary aortic sarcoma often poses diagnostic challenges for pathologists and clinicians because of a very low incidence and controversy over nomenclature and definition. We report a case of aortic angiosarcoma in association with a graft. We also conducted a clinicopathological review of cases of primary aortic sarcomas associated with implanted grafts.

**Case Report:** The patient was an 82-year-old woman. She underwent thoracic endovascular aneurysm repair (TEVAR) at age 78 because of an aneurysm in the descending aorta. Approximately 4 years after the TEVAR, computed tomography revealed a type II endoleak and expansion of the aneurysm. Her c-reactive protein level rose to 34 mg/dL, and Ga scintigraphy showed <sup>67</sup>Ga accumulation at the aneurysm. She had fever up to 39°C, and a stent graft infection was suspected. Despite administration of antibiotics, her condition deteriorated, and she died. Postmortem examination identified epithelioid aortic angiosarcoma at the aorta with aneurysm repair and the graft, and the aortic angiosarcoma invaded the left lower lobe of the lung.

**Conclusions:** Our clinicopathological review revealed that the proper clinical diagnosis was very difficult owing to confusion of aortic sarcoma after the implantation with the infected graft, atypical endoleak, or pseudoaneurysm. The histological diagnosis was ambiguous because immunohistochemical and genetic studies were not adequately conducted. Overall prognosis of aortic sarcoma is poor as most patients die within a year, with no effective treatments. It is hoped that recent projects for genomic medicine will provide useful insights about the diagnosis and treatment of these cancers.

**Keywords:** Aorta • Autopsy • Blood Vessel Prosthesis • Sarcoma

Full-text PDF: <https://www.amjcaserep.com/abstract/index/idArt/931740>

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## Background

More than 160 cases of primary aortic sarcoma have been reported and two-thirds of them originated in the intima [1]. When sarcomas arise in the intima of great vessels of systemic and pulmonary circulation, they are conventionally classified as intimal sarcoma [2,3]. At least 70 cases of intimal sarcoma of the aorta have been reported in the English-language literature [2]. Serious diagnostic challenges for pathologists as well as clinicians still exist in the classification of primary sarcomas of great vessels owing to their very low incidence and controversy over nomenclature and definition [4-6]. Meanwhile, aortic sarcoma is rarely associated with implanted aortic grafts used in repair of aortic aneurysms. Over 20 cases have been reported, according to a search of the Medline database (Tables 1, 2) [7-26].

In this paper, we report a case of aortic angiosarcoma in association with an aortic graft that was recognized in the postmortem examination. We also conducted a comprehensive, clinicopathological review of the cases that have been reported as primary aortic sarcomas associated with implanted grafts. In the discussion, we address several issues related to aortic sarcomas, such as histological classification, clinicopathological features, and updated genomic information.

## Case Report

### Clinical Summary

The patient was an 82-year-old woman. Her past medical history included tuberculosis at age 20, appendicitis at age 30, asthma at age 50, and acute cholecystitis at age 79. She had been on hemodialysis for 20 years for renal failure, likely caused by glomerulonephritis at age 37. She was found to have mitral valve regurgitation and low cardiac function at age 72. She complained of chest pain at age 76. Computed tomography (CT) identified an aortic aneurysm in the thoracoabdominal aorta. She underwent aortic replacement with a prosthetic graft. Another aneurysm of 6.5 cm in diameter was identified in the thoracic descending aorta at age 78. The aneurysm was repaired with thoracic endovascular aneurysm repair (TEVAR). Approximately 4 years after the TEVAR and 2 months before death, a type II endoleak and increase of the aneurysm diameter by 1 cm were identified by CT (Figure 1). C-reactive protein (CRP) was 1 to 2 mg/dL at the time of the TEVAR and showed a gradual increase: 5 to 6 mg/dL, 13 mg/dL, and 34 mg/dL at 8 months, 2 months, and 1 month before death, respectively. The patient was hospitalized for intensive examination and treatment 40 days prior to death. She had an intermittent fever of up to 39°C during hospitalization. Although CRP levels remained high, procalcitonin was 0.73 ng/mL and 1.73 ng/mL

(cut off value was 0.3 ng/mL) 1 month and 2 days before death, respectively.  $\beta$ D-glucan was within normal limits and blood cultures were negative. Nevertheless, culture of pus from her oral cavity demonstrated *Candida albicans* 1 week prior to death. No vegetation was seen on the heart valves by echocardiography. Thrombus in the right pulmonary artery was identified by CT. Ga scintigraphy indicated  $^{67}\text{Ga}$  accumulation at the repaired aorta with the stent graft. Antibiotics were administered on suspicion of stent graft infection. However, the patient's physiological state deteriorated, and she died. Postmortem examination was performed.

### Pathological Findings

An autopsy was performed to confirm (1) the stent graft infection and its cause and (2) the cause of death. Macroscopically, there was a hemorrhagic, 10×6.5×2-cm, crescent-shaped mass with brownish color along the aortic wall. The tumor was compressed and adhered to the mediastinal pleura of the left lower lobe of the lung. A thin layer of coagulated blood and fibrin exudate appeared to cover the intimal surface of the mass (Figure 2A). Histologically, pleomorphic atypical cells proliferated along hemorrhagic spaces or slit-like channels. The neoplastic cells were located on the intima of the aneurysm wall and invaded the aortic tunica media and externa and partially into pulmonary tissue beyond the pleural elastic membrane (Figure 2B). The tumor cells were round or oval in shape and had abundant eosinophilic cytoplasm with large, vesicular nuclei and prominent nucleoli (Figure 3A, 3B). The neoplasm was extensively necrotic with many neutrophils and macrophages.

Immunohistochemically, almost all the neoplastic cells strongly expressed vimentin and CD31, and most of them positively expressed ERG, Factor VIII, and AE1/AE3 (Figure 3C, 3D), but they were negative for CD34 and TTF-1. The neoplasm was diagnosed as epithelioid aortic angiosarcoma of the aorta at the stent graft. VEGFR3 and CDK4 were weakly positive, and MDM2 and C-MYC were completely negative.

No metastasis to other organs was found. Mild to moderate bronchopneumonia was found in the bilateral lungs. Microscopic abscesses were seen in the lung, heart, and liver. Moreover, small amounts of *Candida spp.* were confirmed with Grocott stain in the left and right upper pulmonary lobes and left ventricular myocardium. Although the fungus or bacterial body was not observed in the tumor, the culture from the tumor grew out *Candida albicans*. The heart showed hypertrophy (552 g) and had small foci of fibrosis. The mitral valve and aortic valve showed moderate hyalinization and calcification, but no vegetation was found. The liver was also mildly hypertrophic (1336 g) and showed severe congestion. The kidneys showed severe atrophy (right, 65 g; left, 53g) because of long-standing hemodialysis. Taken together, the cause of

**Table 1.** Clinical features of reported cases with aortic sarcoma associated with aortic prostheses.

Author/ Year	Reference	Sex	Age	Surgical procedures	Graft material	Site of aneurysm	Time to the tumor detection*
O'Connell TX, 1976	7	M	59	AR	Dacron	AA	4 ms
Weinberg DS, 1980	8	M	48	AR	Dacron	TA	14 ms
Fehrenbacher JW, 1981	9	M	67	AR	Dacron	AA	12 ys
Peterson HS, 1989	10	M	57	AR	Dacron	TA	6 ms
Weiss WM, 1991	11	M	56	AR	Dacron	AA	3 ys 6 ms
Fyfe BS, 1994	12	M	70	AR	Dacron	TA	4 ys
Ben-Izhak O, 1999	13	M	71	AR	Dacron	AA	8 ys
Okada M, 2004	14	M	50	AR	Dacron	TA	17 ys
Umscheid TW, 2007	15	M	50	EVAR	Dacron	AA	4 ys 8 ms
Alexander JJ, 2007	16	M	66	AR	Dacron	AA	16 ms
Garg N, 2012	17	M	56	EVAR	Dacron	AA	6 ys
Schmehl J, 2012	18	M	85	EVAR	Dacron	AA	7 ys
Stewart B, 2013	19	M	86	EVAR	Dacron	AA	9 ys
Fenton J, 2014	20	M	72	EVAR	Dacron	AA	6 ys
Kimura S, 2015	21	M	78	AR	Dacron	TA	16 ys
Milite D, 2016	22	M	60	EVAR	PTFE	AA	7 ys
Kamran M, 2016	23	M	69	EVAR	N.D.	AA	8 ys
Kamran M, 2016	23	M	77	EVAR	N.D.	AA	N.D.
Kamran M, 2016	23	F	72	EVAR	N.D.	AA	6 ms
Whittington EA, 2019	24	M	78	EVAR	ePTFE	AA	10 ys
Yu PC, 2019	25	M	68	EVAR	ePTFE	AA	4 ys
Natsume K, 2019	26	M	54	EVAR	Dacron	TA	17 ys
Current case		F	82	EVAR	ePTFE	TA	4 ys
Clinical diagnosis or suspicion							
Author/ Year	Graft infection	Endoleak	Aneurysm**/ pseudoa- neurysm		Mass***	Organ metastasis	Treatment for sarcoma
O'Connell TX, 1976						No	C+R
Weinberg DS, 1980				Yes		No	No
Fehrenbacher JW, 1981				Yes		Lung, liver, penis	C+R
Peterson HS, 1989	Yes					N.D.	R
Weiss WM, 1991					Yes	Liver	C+R
Fyfe BS, 1994				Yes		No	No
Ben-Izhak O, 1999					Yes	Peritoneal dissemination	C
Okada M, 2004						Brain	No

**Table 1 continued.** Clinical features of reported cases with aortic sarcoma associated with aortic prostheses.

Author/ Year	Clinical diagnosis or suspicion				Organ metastasis	Treatment for sarcoma
	Graft infection	Endoleak	Aneurysm**/ pseudoa- neurysm	Mass***		
Umscheid TW, 2007	Yes				Lung and other multiple organs	C
Alexander JJ, 2007			Yes		No	No
Garg N, 2012	Yes	Yes			Liver, lymph nodes	No
Schmehl J, 2012	Yes	Yes			Bone	No
Stewart B, 2013		Yes			Skin, bone	No
Fenton J, 2014	Yes	Yes			Bone	C+R
Kimura S, 2015	Yes		Yes		N.D.	No
Milite D, 2016	Yes	Yes			Peritoneal dissemination	No
Kamran M, 2016		Yes		Yes	No	C+R
Kamran M, 2016				Yes	Multiple organs	No
Kamran M, 2016	Yes		Yes		Gluteal musculature	C
Whittington EA, 2019		Yes			Liver	No
Yu PC, 2019	Yes	Yes			Lymph nodes, possibly	C
Natsume K, 2019					Kidney, bone	No
Current case	Yes	Yes			No	No

In site of aneurysm, descending aorta in thoracic aorta and infrarenal aorta in abdominal aorta was most. \* Time to the tumor detection after surgery; \*\* newly developed aneurysm; \*\*\* mass indicating a possible neoplasm. AR – aortic replacement with prosthetic graft; EVAR – endovascular aortic repair; N.D. – not described; ePTFE – expanded polytetrafluoroethylene; AA – abdominal aorta; TA – thoracic aorta; C – chemotherapy; R – radiation therapy; ms – months; ys – years.

death was multiple organ failure attributable to renal and cardiac failure, intermittent fever, and systemic fungal infection.

## Discussion

Sarcomas of the great vessels of the systemic and pulmonary circulation usually arise in the intima and exhibit primarily intraluminal growth [2,3]. Accordingly, the term intimal sarcoma is often employed for these tumors. The definition by the AFIP acknowledges tumors with any specific types of histology as intimal sarcomas when they arise from the intima of the great vessels [2]. However, the WHO in 2019 defined intimal sarcomas as morphologically non-distinctive, poorly differentiated malignant mesenchymal tumors with or without heterologous elements such as neoplastic cartilage, tumor osteoid, or focal rhabdomyosarcomatous or angiosarcomatous

features [3]. The WHO further maintains that intimal sarcoma has strong nuclear expression of MDM2 protein and high-level amplification of *PDGFRA* and *MDM2*, as demonstrated by fluorescence in situ hybridization (FISH). However, other types of sarcoma such as angiosarcoma are negative for MDM2 and rarely show amplification of *PDGFRA* and *MDM2*, although there are no comprehensive immunohistochemical and genetic studies on these tumors owing to their rarity [27-29]. It raises the question whether intimal sarcoma without MDM2 protein expression or amplification of the genes is excluded from the category and should be classified as another type of sarcoma. Authors of a recent paper have made a proposal for classification of intimal sarcomas to handle this problem [30], stressing that CD31, ERG, or FLI-1 as endothelial (angiosarcoma) markers and MDM2, CDK4, or PDGFRA as poorly differentiated intimal sarcoma markers are essential for proper classification, while molecular examination for amplification

**Table 2.** Clinicopathologic features of reported aortic angiosarcomas associated with aortic prostheses.

Author/Year	Reference	Sex	Age	Surgical procedures	Site of aneurysm	Size of tumor
O'Connell TX, 1976	7	M	59	AR	AA	7 cm
Weinberg DS, 1980	8	M	48	AR	TA	7.4×1.5×2 cm
Fehrenbacher JW, 1981	9	M	67	AR	AA	6×2.4 cm
Peterson HS, 1989	10	M	57	AR	TA	N.D. (a large mass)
Weiss WM, 1991	11	M	56	AR	AA	6×4×3.5 cm
Fyfe BS, 1994	12	M	70	AR	TA	N.D.
Ben-Izhak O, 1999	13	M	71	AR	AA	5.5×4.5 cm*
Okada M, 2004	14	M	50	AR	TA	N.D.
Umscheid TW, 2007	15	M	50	EVAR	AA	N.D.
Alexander JJ, 2007	16	M	66	AR	AA	1.6×0.8 cm
Garg N, 2012	17	M	56	EVAR	AA	N.D.
Schmehl J, 2012	18	M	85	EVAR	AA	N.D.
Stewart B, 2013	19	M	86	EVAR	AA	N.D.
Fenton J, 2014	20	M	72	EVAR	AA	N.D.
Kimura S, 2015	21	M	78	AR	TA	4.5×3 cm*
Milite D, 2016	22	M	60	EVAR	AA	10.2 cm
Kamran M, 2016	23	M	69	EVAR	AA	3.1×2.4 cm
Kamran M, 2016	23	M	77	EVAR	AA	N.D.
Kamran M, 2016	23	F	72	EVAR	AA	7.3 cm
Whittington EA, 2019	24	M	78	EVAR	AA	8.4 cm
Yu PC, 2019	25	M	68	EVAR	AA	4.2 cm
Natsume K, 2019	26	M	54	AR	TA	4.0×2.2×2 cm
Current case		F	82	EVAR	TA	10×6.5×2 cm

Author/Year	Histology		Outcome	Time to outcome**	Autopsy
	Histological diagnosis	Immunohistochemistry			
O'Connell TX, 1976	FS	N.D.	Dead	14.5 ms	Yes
Weinberg DS, 1980	MFH	N.D.	Perioperative death	2 ms	Yes
Fehrenbacher JW, 1981	AS	N.D.	Dead	7 ms	Yes
Peterson HS, 1989	MFH	N.D.	Dead	12 ws	No
Weiss WM, 1991	AS	+ve: vimentin, Factor VIII; –ve: cytokeratins	Alive	15 ms	–
Fyfe BS, 1994	pMFH	N.D.	Perioperative death	a few ms	Yes
Ben-Izhak O, 1999	eAS	+ve: CD31, CD34, Factor VIII, AE1/AE3, CAM5.2	Dead	6 ms after diagnosis	N.D.
Okada M, 2004	AS	+ve: CD31, –ve: CD34, Factor VIII	Dead	2 ws	Yes
Umscheid TW, 2007	eAS	+ve: Factor VIII, CD34; –ve: cytokeratins	Dead	24 ms	N.D.
Alexander JJ, 2007	IS	+ve: vimentin, pancytokeratin; –ve: CD31, CD34, Factor VIII, desmin, SMA, cytokeratin 8/18, EMA	Perioperative death	N.D.	No
Garg N, 2012	IS	+ve: CD31, Fli-1, CK7; –ve: CK20	Dead	6 ws after discharge	N.D.

**Table 2 continued.** Clinicopathologic features of reported aortic angiosarcomas associated with aortic prostheses.

Author/Year	Histology		Outcome	Time to outcome**	Autopsy
	Histological diagnosis	Immunohistochemistry			
Schmehl J, 2012	eAS	+ve: CD31, pancytokeratin, P53 (10%); –ve: CD30, EMA, CD34	N.D.	N.D.	N.D.
Stewart B, 2013	AS	+ve: vimentin, CD31; –ve: CD34, desmin, SMA, pancytokeratin	Dead	3 ms after last surgery	Yes
Fenton J, 2014	AS	N.D.	Dead	1 ms after diagnosis	Yes
Kimura S, 2015	AS	N.D.	Dead	2 ms after treatment	Yes
Milite D, 2016	eAS	+ve: vimentin, CD31, CD34, Factor VIII	Dead	1 ms and 3 ws	N.D.
Kamran M, 2016	eAS	N.D.	Alive	15 ms after treatment	–
Kamran M, 2016	eLS	N.D.	Dead	N.D.	N.D.
Kamran M, 2016	AS	+ve: CD31	Alive	N.D.	–
Whittington EA, 2019	SPS	N.D.	Dead	Several ms	N.D.
Yu PC, 2019	eAS	N.D.	Alive	2 ms after last surgery	–
Natsume K, 2019	IS	+ve: CD31, MDM2	Dead	5 ms and 20 ds	No
Current case	eAS	+ve: vimentin, CD31, Factor VIII, ERG, pancytokeratin, CDK4; –ve: MDM2	Dead	8 ms	Yes

AR – aortic replacement with prosthetic graft; EVAR – endovascular aortic repair; AA – abdominal aorta; TA – thoracic aorta; N.D. – not described; FS – fibrosarcoma; MFH – malignant fibrous histiocytoma; AS – angiosarcoma; pMFH – pleomorphic malignant fibrous histiocytoma; eAS – epithelioid angiosarcoma; eLS – epithelioid leiomyosarcoma; SPS – spindle and pleomorphic sarcoma; +ve – positive; –ve – negative; ds – days; ws – weeks; ms – months. \* Measure on the figure in original paper; \*\* as far as can be determined from original paper. Time from symptom onset to outcome for those not annotated.

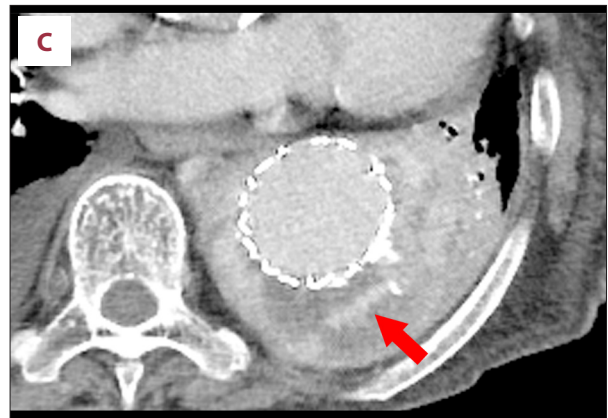
of *MDM2* and *PDGFRA* are required in immunophenotypically ambiguous cases.

Regarding aortic intimal sarcoma, at least 70 cases have been reported, according to the AFIP [2]. Over half of the cases were classified as aortic angiosarcoma, followed by poorly differentiated sarcomas of fibroblastic or myofibroblastic differentiation. Rustoven et al have done a systematic review of aortic sarcomas through a search of the Medline database [1]. Among the 165 cases they identified, the most common site of origin was the aortic intima (110, 66.7%). Undifferentiated tumor histology was most common (65, 39.4%), followed by vascular (61, 37%) and smooth muscle (22, 13.3%). However, most of the cases have been reported in the radiologic or surgical literature without thorough immunohistochemical or molecular analysis. There are only a few reports of immunohistochemical studies with *MDM2* and *CDK4* and analysis by FISH of *MDM2* and *PDGFRA* amplification for aortic intimal sarcoma including the undifferentiated, vascular, and other type of

tumors [28,29]. Detailed clinicopathologic, immunohistochemical, and molecular analyses are required for classifying and reporting cases of aortic intimal sarcoma.

Aortic sarcoma in association with an implanted aortic graft is very rare. To the best of our knowledge, 23 cases, including the present case, have been reported, as listed in **Tables 1 and 2**. The patient ages ranged from 48 to 86 years with an average of 66.6 years. Female to male ratio is 2: 21. The site of the repaired aneurysm was thoracic aorta in 7 cases and abdominal aorta in 16 cases. Patients most frequently reported a wide variety of nonspecific symptoms such as general fatigue, abdominal pain, weight loss, and fever. The proper clinical diagnosis was very difficult owing to frequent confusion of aortic sarcoma after implantation of graft with the infected graft (10/23), atypical endoleak (9/23), or pseudoaneurysm (6/23) while mass (4/23) was suspected on imaging. Although all of the conditions can have overlapping features with sarcoma, they are more likely to be suspected than sarcoma since





**Figure 1.** (A) Non-contrast, (B) arterial-phase, and (C) delayed post-contrast computed tomography images. They showed a crescent-shaped aortic aneurysm with endoleak (red arrows), approximately 6 cm in size, surrounding the stent graft.

they are clinically much more common [23]. However, no patients who were suspected of having an infected graft finally demonstrated positive blood or tissue culture or evidence of purulence. Accordingly, clinical suspicion of infection may have been attributable to neoplastic fever. Over a dozen papers have indicated that neoplastic fever ranges from 7.0% to 35.4% in frequency among patients with malignancy [31]. Nakamura et al reported that neoplastic fever was observed in 11 (5.6%) of 195 patients with bone and soft tissue sarcomas [32]. Neoplastic fever in the setting of aortic sarcoma requires further investigation.

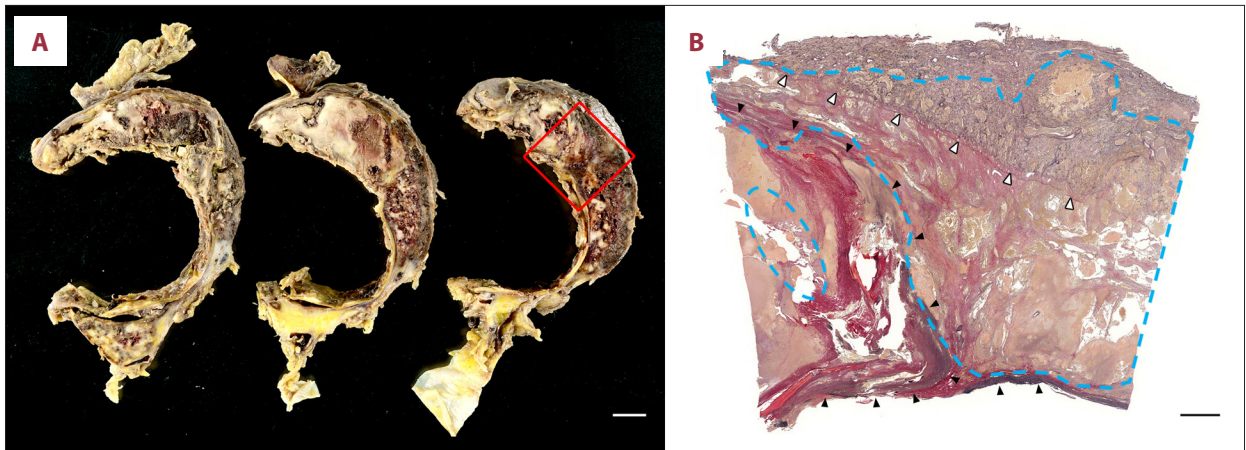
It is reported that 10% of patients with aortic intimal sarcoma present with an abdominal aortic aneurysm [2]. Another study reported that 26.7% of 165 aortic sarcomas were misattributed to aneurysm/pseudoaneurysm [1]. Consequently, diagnosis of aortic sarcomas associated with aneurysm repair is difficult. As shown in **Tables 1 and 2**, the time to development or detection of intimal aortic sarcoma after surgery ranges from 4 months to 17 years. The time of the two different surgical procedures seems to be similar in length. There is no certain evidence of the tumor growth rate in the aorta, where neoplastic conditions are exceedingly rare. However, the tumors that developed within 6 months after surgery most likely existed in the treated aorta because all were large in size at the time of detection; one that arose at 4 months was 7.0 cm, another

that was found at 6 months was 7.3 cm, and the other case that was identified at 6 months was described as a large tumor.

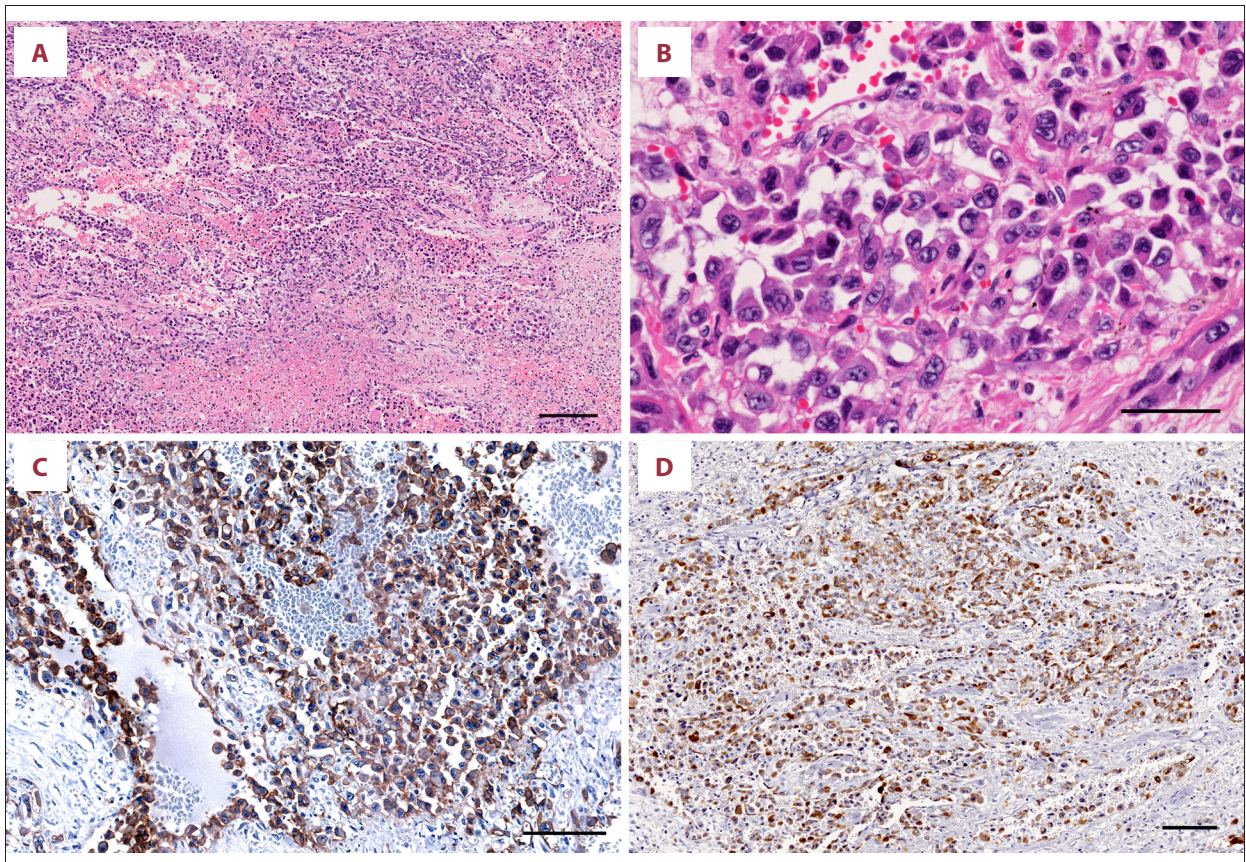
To repair an aortic aneurysm, open surgery, namely aortic replacement with a prosthetic graft, was the most common technique until early 2000. A minimally invasive surgery, endovascular aneurysm repair, was introduced three decades ago and is now the dominant treatment, as demonstrated in **Table 1**. A case series with aortic intimal sarcoma [5] and another with aortic sarcoma [1] showed similar frequencies of sarcomas in association with synthetic prostheses, with frequencies of 4.5% and 6.7%, respectively. These numbers suggest that there did not seem to be a strong correlation between these sarcomas and the synthetic graft. Some reports indicated that the association could be coincidental because there were very small number of cases with tumors, in comparison with the large number of cases with therapeutic procedures performed [5,23].

Meanwhile, the graft can increase the likelihood of malignancy secondary to chronic injury/inflammation or some other mechanism [5]. Additionally, in **Table 2**, aortic angiosarcoma is the most common (75% of cases) type of sarcoma associated with the implanted graft, compared with other types of sarcoma, such as undifferentiated sarcomas, although immunohistochemistry analysis was not performed in some cases, limiting the conclusions that can be made. Only a few genomic studies of aortic angiosarcoma demonstrated that some distinct molecular patterns of aortic angiosarcoma occurred at distinct sites: high-level *MYC* amplification in post-radiation and chronic lymphoedema-associated aortic angiosarcoma of the breast [33], activating mutations in *PIK3CA* nearly exclusively in primary breast aortic angiosarcoma, and a dominant mutational signature of ultraviolet exposure with aortic angiosarcoma of the head, neck, face, and scalp [34]. There is a report on





**Figure 2.** (A) Cross-sections of the thoracic descending aortic wall after removal of the stent graft. A crescent-shaped aneurysm-like mass with severe hemorrhage was shown along with aortic wall. This mass corresponded to the lesion shown in **Figure 1**. (B) Elastic van Gieson stain corresponding to the area surrounded by the red square in (A). The tumor (surrounded by blue dashed line) mainly located in the aortic wall and destroyed aortic media (black arrowheads) and focally invaded into the lung through the pleura (white arrowheads). Below the pleura was the aortic wall and above the pleura was the left lower lobe of the lung. Bars, (A) 10 mm, (B) 2 mm.



**Figure 3.** (A, B) Hematoxylin and eosin stain of the tumor. The tumor cells formed (A) a sinusoidal pattern with hemorrhage, fibrin deposition, thrombi, and necrosis and showed (B) severe cellular atypia and appeared to have an intercellular adhesive property which suggested epithelioid features. (C) CD31 and (D) AE1/AE3 stain of the tumor. The tumor cells were positive for CD31, indicating vascular endothelial differentiation, and AE1/AE3, meaning epithelioid feature. Bars, (A, D) 200  $\mu$ m, (B) 50  $\mu$ m, (C) 100  $\mu$ m.



genetic profiles of aortic angiosarcoma showing *MYC* amplification in one of the three cases [28]. While intimal sarcomas in the pulmonary artery often display gains or amplifications of 12q12-q15 (*CDK4*, *TSPAN31*, *MDM2*, *GLI1*) [35-37], the molecular signatures have been rarely studied in aortic sarcomas. Further genetic studies are needed to elucidate whether there is a strong association between the graft and aortic sarcomas.

Prognosis of aortic sarcoma in association with an implanted graft is poor, as most patients died within a year after diagnosis, as shown in **Table 2**. Since the clinical and/or histological diagnoses can be extremely difficult, the tumor can rapidly progress before a definitive diagnosis is made. Consequently, a novel diagnostic method to detect the tumor in an early and precise manner would be useful. There are recent studies on the potential role of microRNAs in diagnosing sarcomas [38,39]. Rare cancers like aortic angiosarcoma are a significant unmet clinical need because they have limited large-scale clinical and genomic studies. To overcome these challenges, the Angiosarcoma Project was initiated in the United States and Canada, generating genomic data [34]. In Japan, the Master Key Project started in 2017 at the National Cancer Center [40] to promote genomic medicine in rare cancers. It is hoped that these dedicated projects will provide useful insights about the diagnosis and treatments of these rare cancers.

## Conclusions

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We reported a rare autopsy case of angiosarcoma that arose in the thoracic descending aorta that had been treated with a stent graft 4 years before. Since the patient's main symptoms and clinical data were high fever, high CRP level, and type II endoleak, such nonspecific findings could not lead us to a sarcoma as an antemortem diagnosis. Reviewing this case and related literature, we believe that detailed clinicopathologic, immunohistochemical, and molecular analyses, as well as accumulation of accurate data, are important to develop a novel diagnostic and treatment method to detect such rare tumors.

## Acknowledgements

We thank Yukari Goto, MD for her advice on radiological imaging of this case report.

## Conflicts of Interest

None.

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